-- A method is disclosed for determining whether a compound binds to a lipoprotein such as LDL or VLDL in a manner which will lower plasma cholesterol. The method provided includes assessing the ability of the compound to form a complex with the lipoprotein, and then determining whether the newly formed complex causes a change in the structure of apoB-100 that results in increased binding affinity to an LDL receptor.--

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Information Disclosure Statement

A full translation of French Patent No. 2.168.137 which is the most representative of the French patent documents AQ-AV listed on the original information disclosure statement is provided on the attached supplemental Information Disclosure Statement (PTO Form 1449).

In the Claims

Applicants amend claims 1, 4-6, 9, 15, 21-24, 25, 26 and 29-36. Applicants provide the text of the amended claims below and then attach a marked-up version of the original claims that indicates the amendments.

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1. (Twice Amended) A method to assess whether a compound first binds to and then enhances the clearing of a cholesterol-containing low density lipoprotein (LDL) after subsequent binding to the low density lipoprotein receptor in a host human or other animal comprising:

(a) administering the compound to the host,

(b) isolating the cholesterol-containing low density lipoprotein from the host,

(c) determining whether the binding of the compound to the cholesterol-containing low density lipoprotein forms a complex; and

(d) determining whether the complex results in a change in the three dimensional conformation of the lipoprotein that enhances the binding affinity of the lipoprotein to the low density lipoprotein receptor.

4. (Amended) The method of claim 1, wherein the binding of the compound to the cholesterol-containing low density lipoprotein is assessed by a sandwich immunoreactivity assay.

5. (Amended) The method of claim 1, wherein the binding of the compound to the cholesterol-containing low density lipoprotein is assessed using agarose electrophoresis.

6. (Twice Amended) A method to determine whether a compound first binds to and then increases the clearance of a low density lipoprotein after subsequent binding to the low density lipoprotein receptor in a host, comprising

(i) mixing the compound with low density lipoprotein;

(ii) determining whether the compound binds to the low density lipoprotein and forms a complex; and

(iii)determining whether the complex alters the three dimensional conformation of the lipoprotein such that the binding of the lipoprotein to a lipoprotein receptor is enhanced.

9. (Twice Amended) A method to determine if a compound causes a change in the structure of apolipoprotein B-100 in a cholesterol-containing low density lipoprotein, wherein, an epitope on the apolipoprotein B-100 binds to an LDL-receptor, comprising:

(i) mixing the compound with and allowing it to bind to low density lipoprotein;

(ii) carrying out a sandwich immunoreactivity assay on the compound-low density lipoprotein mixture using a first antibody directed to the epitope on apolipoprotein B-100 that binds to the LDL-receptor,

(iii) using a second, capture antibody that is attached to a solid phase and which binds to the first antibody;

(iv) detecting the second capture antibody bound to the first antibody

(v) quantifying the amount of the first antibody - LDL - compound captured by the second antibody; and

(vi) comparing the amount of LDL captured by the assay to a control.

15. (Twice Amended) A method for assessing whether a compound first binds to a lipoprotein, enhancing the binding of the lipoprotein to a low density lipoprotein hepatic receptor and thus lowering plasma cholesterol, the method comprising:

(a) allowing the compound to form a complex with a cholesterol-containing lipoprotein in vivo,

(b) isolating the resulting complex, and

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(c) determining whether the formation of the complex causes a change in the three dimensional conformation of apoB-100 in the lipoprotein that enhances the binding of the lipoprotein to the LDL hepatic receptor.

21. (Amended) The method of claim 2, wherein the apolipoprotein is apoB-100.

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22. (Amended) The method of claim 1, wherein the lipoprotein receptor is hepatic.

Sub. D5

23. (Amended) The method of claim 6, wherein the lipoprotein is VLDL.

25. (Amended) The method of claim 6, wherein the determination of whether the compound binds to the low-density lipoprotein and forms a complex is assessed by a sandwich immunoreactivity assay.

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26. (Amended) The method of claim 6, wherein the determination of whether the compound binds to the low-density lipoprotein and forms a complex is assessed using agarose electrophoresis.

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29. (Amended) The method of claim 9, wherein the control is cholesterol-containing low density lipoprotein in the absence of test compound.

Sub. D6

30. (Amended) The method of claim 10, wherein the cholesterol-containing low-density lipoprotein is VLDL.

31. (Amended) The method of claim 15, wherein the formation of the complex is determined by a sandwich immunoreactivity assay.

32. (Amended) The method of claim 15, wherein the formation of the complex is determined using agarose electrophoresis.

~~33. (Amended) The method of claim 9, wherein the apolipoprotein is apoB-100.~~

~~34. (Amended) The method of claim 9, wherein the lipoprotein-receptor is a low-density~~ lipoprotein (LDL) receptor.

Sub D2

35. (Amended) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is LDL.

C9 cont

36. (Amended) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is VLDL.